**Supporting Information**

# Copper-Catalyzed Functionalization of Benzylic C–H Bonds with *N*-Fluorobenzenesulfonimide (NFSI): Switch from C–N to C–F Bond Formation Promoted by a Redox Buffer and Brønsted Base

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## Table of Contents

## I. General Considerations

All reagents were purchased from commercial sources and used as received. Nearly identical performance was observed when using reagents from different commercial sources. Cu salts were purchased from Strem Chemicals and Sigma-Aldrich. C–H substrates were purchased from Oakwood, Combi-Blocks, TCI America, Ambeed, or Sigma-Aldrich. NFSI was purchased from Ark-Pharm and Oakwood. Bathophenanthroline was purchased from Aldrich and Ambeed. $MeB(OH)_2$ was purchased from Sigma-Aldrich and Combi-Blocks.

All fluorination reaction solids were weighed out on the benchtop, while liquids were added in an inert atmosphere ($N_2$) glovebox. Retention in performance can be obtained by setting up the fluorination reaction on the benchtop with backfilling or sparging of the reaction vessel with $N_2$. $^1H$, $^{13}C$, and $^{19}F$ NMR spectra were recorded on a Bruker Avance III 400 spectrometer at 25 °C ($^1H$ 400.1 MHz, $^{13}C$ 100.6 MHz, $^{19}F$ 376.5 MHz) or a Bruker Avance III 500 spectrometer at 25 °C ($^1H$ 500.1 MHz, $^{13}C$ 125.7 MHz, $^{19}F$ 470.6 MHz), except where noted otherwise, and chemical shifts are reported in parts per million (ppm). NMR spectra were referenced to residual $CHCl_3$ at 7.26 ppm ($^1H$) and $CDCl_3$ at 77.16 ppm ($^{13}C$). All $^{19}F$ NMR spectra were absolutely referenced to their respective solvent peaks in the $^1H$ NMR spectrum. Chromatography was performed using an automated Biotage Isolera® with reusable 25 g Biotage® Sfär Silica HC D cartridges for normal phase or 60 g Biotage® SNAP Ultra C18 cartridges for reversed phase. UV-visible data were collected with an Agilent Technologies stainless steel DIP probe equipped with a 1 mm Immersion Fiber Optic Probe Tip. High-resolution mass spectra were obtained using a Thermo Q Exactive™ Plus via (ASAP-MS) by the mass spectrometry facility at the University of Wisconsin.

## II. General Procedure for Benzylic C–H Fluorination and NMR Quantitation

*Warning: This reaction evolves gas from protonation of $Li_2CO_3$, which is able to pressurize the reaction vial. Be sure to take appropriate safety precautions.*

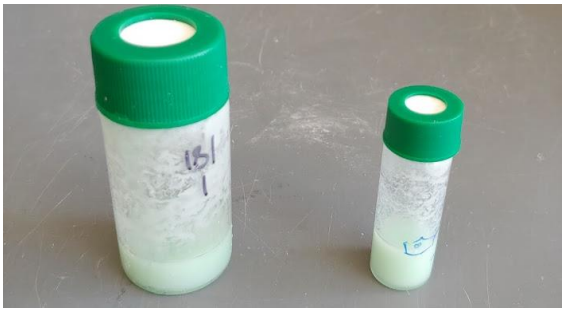
**Set-up:** On the benchtop, a disposable 4 mL glass vial was charged with $MeB(OH)_2$ (0.6 mmol, 35.9 mg, 2 equiv), $Li_2CO_3$ (0.9 mmol, 66.5 mg, 3 equiv), N-fluorobenzenesulfonimide (NFSI; 0.75 mmol, 236.5 mg, 2.5 equiv), and a Teflon stir bar. The vial was sealed by a PTFE-lined pierceable cap. Bathophenanthroline (BPhen, 0.0216 mmol, 7.2 mg, 0.072 equiv) was weighed into a secondary vial with a Teflon stir bar. Both vials were then transferred to a purging glovebox under $N_2$(g). In the glovebox, CuOAc (0.018 mmol, 2.2 mg, 0.06 equiv) was weighed into the vial containing BPhen. Chlorobenzene (1.8 mL) was added to this vial and the vial is stirred to form a deep red 0.01 M stock solution of copper catalyst. The C–H substrate (0.3 mmol, 1 equiv) was weighed into the vial containing the rest of the reaction components, and then 0.6 mL of the copper catalyst solution was transferred to the reaction vial to give a 0.5 M mixture with a 2 mol% catalyst loading. The solution color changes from red to blue/green. This reaction vial is then removed from the glovebox and set to stir at 45 °C on a stir plate at 450 rpm for 16 h.

**Work-up:** At the end of the reaction, the mixture often becomes a light blue paste. The cap of the vial is loosened to vent the pressure build-up from the reaction. Dibromomethane (0.3 mmol, 21 µL, 1 equiv) and trifluorotoluene (0.3 mmol, 37 µL, 1 equiv) are then added as $^1$H and $^{19}$F NMR standards, respectively. The mixture is then diluted with $CDCl_3$ (0.6 mL), mixed, and a 30 µL aliquot is taken and filtered over a 1-inch celite plug directly into an NMR tube using $CDCl_3$ (in a few cases, dilution was done with dichloromethane or $CHCl_3$). The amount of benzyl fluoride product is then quantified relative to the two added internal standards.

*Reaction tip:*

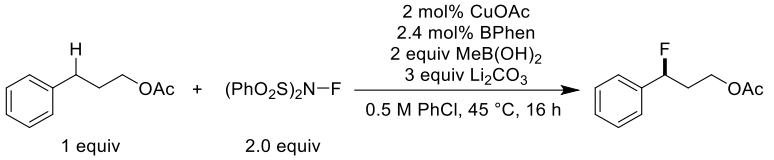
- The fluorination reaction is temperature sensitive, so it is recommended to use a hot plate with a thermocouple.

*Reaction picture:*



## III. Screening Tables

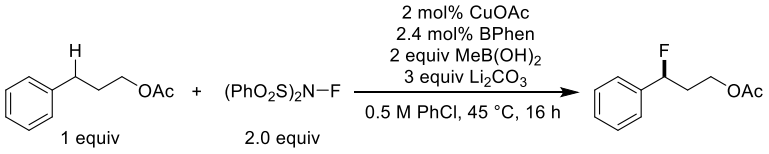
**Table S1.** Control Experiments Table




| entry | control | MB | % SM | % C-N | % C-F($F_2$)[a] |
|---|---|---|---|---|---|
| 1 | No CuOAc | 102 | 102 | -- | -- |
| 2 | No BPhen | 101 | 77 | -- | 24 |
| 3 | No NFSI | 102 | 102 | -- | -- |
| 4 | No $Li_2CO_3$ | 70 | 70 | -- | -- |
| 5 | No $MeB(OH)_2$ | 103 | 103 | -- | -- |
| 6[b] | No $MeB(OH)_2$ w/ 0.5 equiv diisopropyl phosphite | 99 | 95 | -- | 4 |
| 7 | Under Air | 66 | 42 | -- | 24 |

[a]Reactions run at 0.2 mmol scale. Calibrated $^1$H NMR yields using mesitylene as an internal standard. [b]Reaction used 3-phenyl-1-bromopropane as the C–H substrate.

**Table S2.** Reaction Stoichiometry Screening Table




| entry | variation | MB | % SM | % C-N | % C-F($F_2$)[a] |
|---|---|---|---|---|---|
| 1 | standard cond. | 95 | 2 | -- | 80(5) |
| 2 | 35 °C | 93 | 44 | -- | 48(1) |
| 3 | 55 °C | 92 | 3 | -- | 74(10) |
| 4 | 1 equiv. NFSI | 90 | 34 | -- | 52(2) |
| 5 | 3 equiv. NFSI | 98 | 7 | -- | 89(5) |
| 6 | 1 equiv. $Li_2CO_3$ | 95 | 13 | -- | 78(4) |
| 7 | 2 equiv. $Li_2CO_3$ | 93 | 5 | -- | 82(6) |
| 8 | 1 equiv. $MeB(OH)_2$ | 95 | 12 | -- | 79(4) |
| 9 | 2.5 equiv. $MeB(OH)_2$ | 97 | 3 | -- | 87(7) |
| 10 | 1 mol% BPhen | 100 | 12 | -- | 83(5) |
| 11 | 4 mol% BPhen | 103 | 103 | -- | 0 |
| 12 | 1 mol% CuOAc/ 1 mol% BPhen | 96 | 12 | -- | 80(4) |
| 13 | 10 mol% CuOAc/ 10 mol% BPhen | 83 | 13 | -- | 47(3) |
| 14 | 10 mol% CuOAc/ 5 mol% BPhen | 92 | 18 | -- | 63(2) |

[a]Reactions run at 0.2 mmol scale. Calibrated $^1$H NMR yields using mesitylene as an internal standard. Mass balance in this table also accounts for formation of the benzyl ketone.

## IV. Additional Experiments and Observations

### Experiment S1. UV-Visible Titration of NFSI Addition to BPhenCu$^{I}$(OAc)

A 50 mL three-neck round-bottom flask was charged with a stir bar and sealed with two septa and a 90° ground-glass joint. The flask was deoxygenated via three evacuation/refill cycles and placed under an atmosphere of $N_2$. The fiber-optic UV-Visible dip-probe (1 mm path length) was pierced through the center neck of the flask and positioned directly above the stir bar (Figure S1). Degassed PhCl (32 mL) was added to the flask via syringe. The 100% transmittance baseline spectrum was collected.

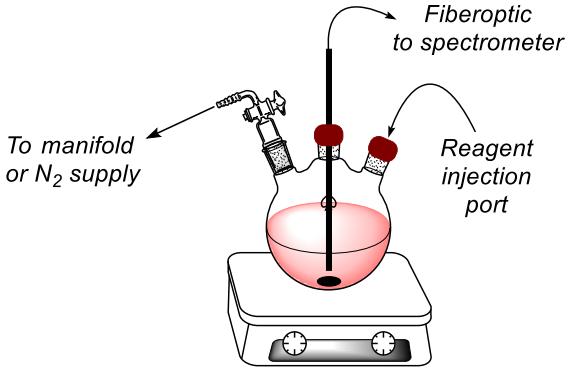



**Figure S1.** Representative schematic for the experimental set-up used in the BPhenCu$^{I}$(OAc)/NFSI titration experiments.

In the glovebox, a stock solution of BPhenCu$^{I}$(OAc) was prepared by dissolving BPhen (40.0 mg, 0.120 mmol) and Cu$^{I}$(OAc) (12.3 mg, 0.100 mmol) in PhCl (10 mL). The resulting deep red solution was loaded into a 1 mL syringe and the needle sealed by septum. A second stock solution of NFSI (31.5 mg, 0.100 mmol) in PhCl (10 mL) was prepared in a septum-capped vial.

The BPhenCu$^{I}$(OAc) solution was injected into the round-bottom flask with a positive counterpressure of $N_2$, affording a homogeneous red/brown solution with a total [Cu$^{I}$] of 0.33 mM. A UV-visible spectrum was collected. With stirring, multiple 100 µL aliquots of the NFSI stock solution was injected (0.001 mmol, 0.1 equiv per aliquot). Spectra were collected after each subsequent addition up to a total of eight additions (Table S3). Isosbestic conversion of Cu$^{I}$ to Cu$^{II}$ is observed through five additions. Additional oxidant resulted in no change to the UV-visible spectrum. Representative wavelengths for Cu$^{I}$ (375 nm) and Cu$^{II}$ (325 nm) were selected for tracking conversion.

**Table S3.** UV-visible data for the Cu/NFSI titration shown in Figure 1B.

| Equiv NFSI | Abs @ 375 nm | Relative % [Cu$^{I}$] | Abs @ 325 nm | Relative % [Cu$^{II}$] |
|---|---|---|---|---|
| 0.0 | 0.218 | 100 | 0.609 | 0.0 |
| 0.1 | 0.183 | 81.6 | 0.653 | 22.8 |
| 0.2 | 0.142 | 61.0 | 0.688 | 41.4 |
| 0.3 | 0.101 | 39.8 | 0.720 | 57.7 |
| 0.4 | 0.059 | 18.2 | 0.755 | 76.2 |
| 0.5 | 0.024 | 0.0 | 0.801 | 100 |
| 0.6 | 0.024 | 0.0 | 0.801 | 100 |
| 0.7 | 0.024 | 0.0 | 0.801 | 100 |
| 0.8 | 0.024 | 0.0 | 0.801 | 100 |

**Experiment S2. UV-Visible Spectroscopic Analysis of NFSI Addition to $Cu^{I}$ in the Presence of $MeB(OH)_2$ and Base**

A 50 mL three-neck round-bottom flask was charged with $MeB(OH)_2$ (3 mg, 0.05 mmol, 5 equiv), $Li_2CO_3$ (11.1 mg, 0.15 mmol, 15 equiv), and a stir bar and sealed with two septa and a 90° ground-glass joint. The flask was deoxygenated via three evacuation/refill cycles (*nb*. care must be taken not to pump off the $MeB(OH)_2$ under high vacuum; *ca.* 200 mtorr is acceptable) and placed under an atmosphere of $N_2$. The reaction vessel was fashioned with the fiber-optic dip-probe analogous to the experimental setup described in Experiment S1 (*cf.* Fig. S1). Degassed PhCl (32 mL) was added to the flask via syringe. The 100% transmittance baseline spectrum was collected.

A deep red $BPhenCu^{I}(OAc)$ stock solution (1 mL at 10 mM) was injected via syringe under a counterflow of $N_2$, affording a homogeneous red/brown solution. A UV-visible spectrum was recorded to benchmark authentic 0.33 mM [$BPhenCu^{I}(OAc)$] (Table S4). With stirring, NFSI (0.005 mmol, 0.5 equiv) was added as a stock solution in PhCl (0.5 mL), resulting in an immediate color change to light blue. UV-visible spectra (270 to 670 nm) were collected at five-minute intervals, monitoring the reduction of $Cu^{II}$ to $Cu^{I}$ (Table S4). The spectra were baseline corrected using the absorbance value at 670 nm, where the copper species present have negligible background absorption.

**Table S4.** UV-visible data for the $MeB(OH)_2$-mediated reduction of $Cu^{II}$ (*cf.* Fig. 1B).

| Time | λ (nm) | | % Recovery of $Cu^{I}$ | Time | λ (nm) | | % Recovery of $Cu^{I}$ |
|---|---|---|---|---|---|---|---|
| | 460 | 670 | | | 460 | 670 | |
| (pre NFSI) | 0.305 | 0.039 | N/A | 60 | 0.247 | 0.042 | 77 |
| 0 | 0.037 | 0.036 | 0 | 65 | 0.254 | 0.041 | 80 |
| 5 | 0.046 | 0.035 | 4 | 70 | 0.257 | 0.041 | 81 |
| 10 | 0.053 | 0.033 | 7 | 75 | 0.261 | 0.042 | 82 |
| 15 | 0.067 | 0.037 | 11 | 80 | 0.265 | 0.042 | 84 |
| 20 | 0.084 | 0.038 | 17 | 85 | 0.266 | 0.040 | 85 |
| 25 | 0.102 | 0.040 | 23 | 90 | 0.268 | 0.040 | 86 |
| 30 | 0.129 | 0.044 | 32 | 95 | 0.271 | 0.042 | 86 |
| 35 | 0.143 | 0.037 | 40 | 100 | 0.271 | 0.040 | 87 |
| 40 | 0.170 | 0.040 | 49 | 105 | 0.271 | 0.040 | 87 |
| 45 | 0.188 | 0.041 | 54 | 110 | 0.273 | 0.042 | 87 |
| 50 | 0.214 | 0.040 | 65 | 115 | 0.274 | 0.040 | 88 |
| 55 | 0.234 | 0.041 | 73 | 120 | 0.276 | 0.039 | 89 |

**Experiment S3. Stoichiometric Reactivity of $MeB(OH)_2$ with NFSI in the Presence of Cu**

According to the UV-visible data, NFSI rapidly oxidizes $Cu^{I}$ to $Cu^{II}$ and $MeB(OH)_2$ slowly reduces the $Cu^{II}$ species back to $Cu^{I}$. One diagnostic product that we attribute to this reduction is the formation of Me–NSI. Me–NSI is readily observed in the optimized fluorination reaction as a singlet near 3.3 ppm in the $^1H$ NMR spectrum.[1]

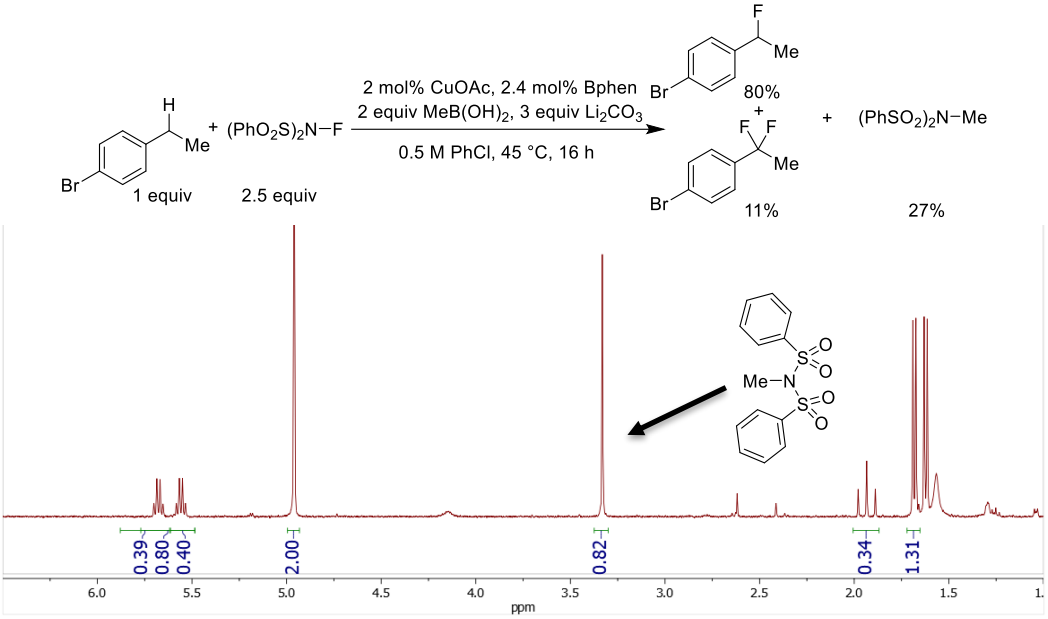



**Figure S2.** $^1H$ NMR Spectrum ($CDCl_3$, 400 MHz, 25 °C) of the fluorination reaction with 0.3 mmol of $CH_2Br_2$ (21 µL) added as an internal standard (4.96 ppm). The alkyl protons from fluorinated products are integrated.

In an independent experiment, we left the C–H substrate out of the reaction and used $MeB(OH)_2$ as the limiting reagent with additional Cu catalyst in solution. These conditions led to a high 78% yield of the methylated sulfonimide.

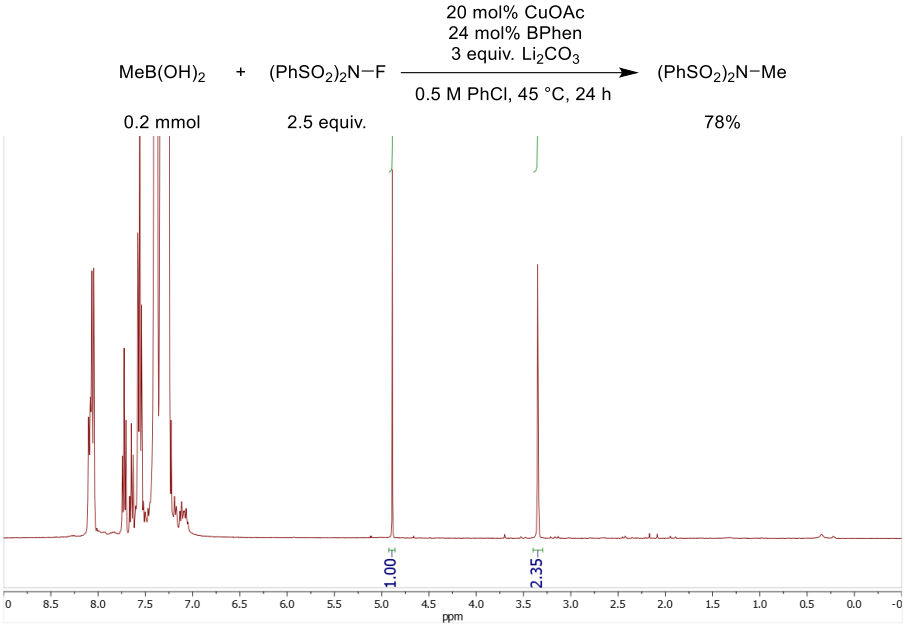



**Figure S3.** $^1H$ NMR Spectrum ($CDCl_3$, 400 MHz, 25 °C) of the fluorination reaction with 0.1 mmol of $CH_2Br_2$ (7 µL) added as an internal standard (4.96 ppm). The Me peak from Me–NSI is integrated.

Based on these observations and on existing mechanistic studies of oxidative Chan-Lam coupling, it is possible that operative reduction pathways for $Cu^{II}$ to $Cu^{I}$ are via a disproportionation reaction and reductive elimination reaction.[2,3]

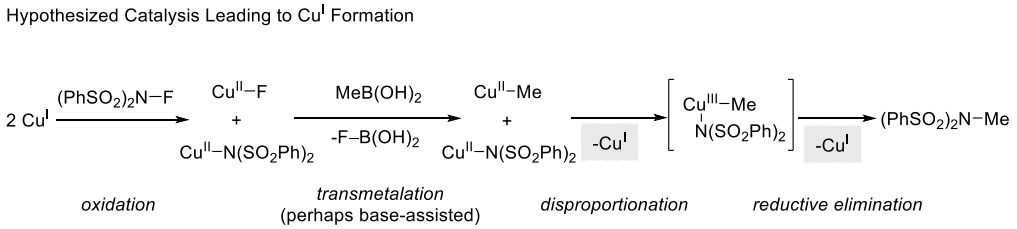



**Figure S4.** A proposed reaction pathway allowing $Cu^{II}$ reduction to $Cu^{I}$ when using $MeB(OH)_2$ as the reductant. This suggested order of operations aligns with the proposed mechanism of Chan-Lam coupling reactions.

**Experiment S4. Time Course Data for Variations of the Optimized Reaction Conditions**

A set of eighteen 1-bromo-4-ethylbenzene fluorination reactions were setup on a 0.3 mmol scale mostly in accord with the general procedure in section II. All of the reactions were placed in a pre-heated heating block (45 °C) on a stir plate set to 750 rpm. At the designated timepoints, reactions were removed from the plate, opened, diluted with 0.5 mL of PhCl and internal standards were added (21 µL $CH_2Br_2$ and 37 µL $PhCF_3$) via micro syringe. The reaction vials were then sealed, mixed vigorously, and a 50 µL aliquot was removed. This aliquot was filtered through a short (ca. 0.5 inch) celite plug with $CDCl_3$ (100 + 300 + 300 µL) directly into an NMR tube. $^1H$ and $^{19}F\{^1H\}$ NMR spectra were collected for each timepoint to track reaction speciation.

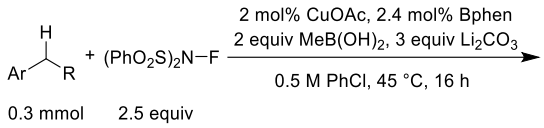



**Table S5.** Time course data for optimized fluorination reaction conditions (*cf.* Figure 1C).

| Time (h) | [C–H] (M) | [C–F] (M) | [C–$F_2$] (M) |
|---|---|---|---|
| 0.08 | 0.49 | 0.02 | 0.00 |
| 0.25 | 0.46 | 0.03 | 0.00 |
| 0.50 | 0.44 | 0.04 | 0.00 |
| 0.75 | 0.43 | 0.06 | 0.00 |
| 1.0 | 0.40 | 0.06 | 0.00 |
| 1.5 | 0.39 | 0.10 | 0.00 |
| 2.0 | 0.36 | 0.14 | 0.00 |
| 2.5 | 0.32 | 0.16 | 0.00 |
| 3.0 | 0.31 | 0.17 | 0.00 |

| Time (h) | [C–H] (M) | [C–F] (M) | [C–$F_2$] (M) |
|---|---|---|---|
| 3.5 | 0.29 | 0.18 | 0.00 |
| 4.0 | 0.26 | 0.22 | 0.00 |
| 4.5 | 0.20 | 0.23 | 0.00 |
| 5.0 | 0.20 | 0.25 | 0.00 |
| 6.0 | 0.17 | 0.27 | 0.01 |
| 7.0 | 0.13 | 0.32 | 0.01 |
| 8.0 | 0.08 | 0.36 | 0.02 |
| 12.0 | 0.03 | 0.40 | 0.03 |
| 16.0 | 0.01 | 0.42 | 0.05 |

A second set of eighteen 1-bromo-4-ethylbenzene fluorination reactions were set up on a 0.3 mmol scale according to the general procedure in section II, except $Li_2CO_3$ was omitted. These vials were placed on a pre-heated block (45 °C) on a stir plate set to 750 rpm. The reactions were processed analogously to those described above (at the same time intervals), providing a kinetic profile for reactions run in the absence of $Li_2CO_3$ (Figure S5).


**Table S6.** Time course data for an optimized fluorination reaction run in the absence of base (*cf.* Scheme 2A).

| Time (h) | [C–H] (M) | [C–F] (M) | [C–OH] + [C=O] (M) | [C–N] (M) |
|---|---|---|---|---|
| 0.08 | 0.50 | 0.01 | 0.00 | 0.00 |
| 0.25 | 0.49 | 0.02 | 0.01 | 0.01 |
| 0.50 | 0.45 | 0.02 | 0.01 | 0.01 |
| 0.75 | 0.44 | 0.03 | 0.01 | 0.02 |
| 1.0 | 0.43 | 0.03 | 0.02 | 0.02 |
| 1.5 | 0.40 | 0.05 | 0.02 | 0.03 |
| 2.0 | 0.36 | 0.05 | 0.04 | 0.03 |
| 2.5 | 0.34 | 0.07 | 0.05 | 0.04 |
| 3.0 | 0.29 | 0.07 | 0.06 | 0.05 |

| Time (h) | [C–H] (M) | [C–F] (M) | [C–OH] + [C=O] (M) | [C–N] (M) |
|---|---|---|---|---|
| 3.5 | 0.27 | 0.08 | 0.09 | 0.08 |
| 4.0 | 0.25 | 0.08 | 0.08 | 0.08 |
| 4.5 | 0.22 | 0.05 | 0.10 | 0.09 |
| 5.0 | 0.21 | 0.03 | 0.09 | 0.08 |
| 6.0 | 0.16 | 0.01 | 0.16 | 0.11 |
| 7.0 | 0.13 | 0.00 | 0.18 | 0.12 |
| 8.0 | 0.10 | 0.00 | 0.24 | 0.13 |
| 12.0 | 0.07 | 0.00 | 0.26 | 0.13 |
| 16.0 | 0.03 | 0.00 | 0.26 | 0.13 |

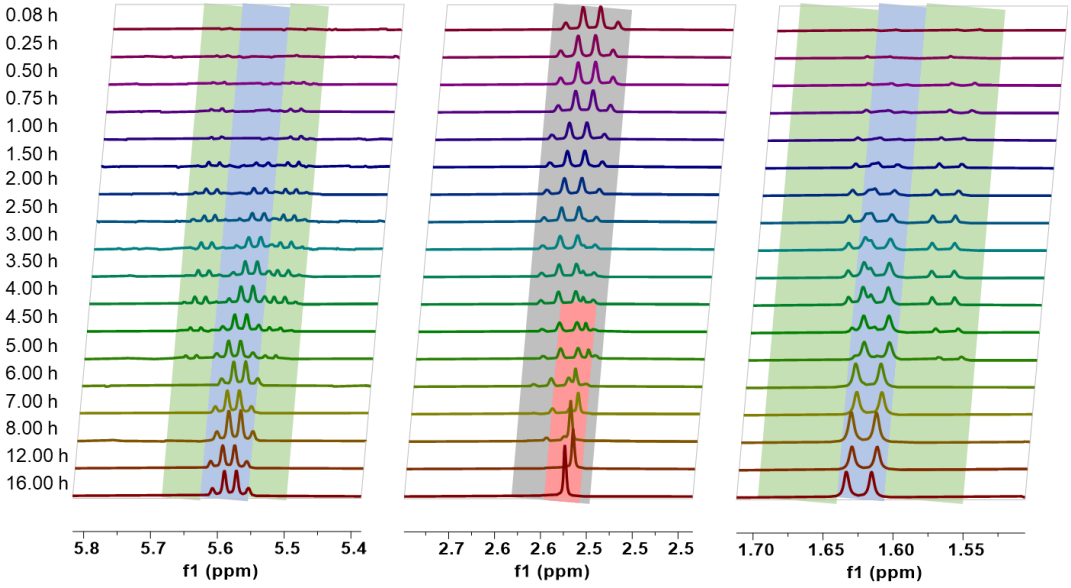



**Figure S5.** Partial $^1$H NMR spectrum (400 MHz, 25 °C) with representative time course data for an optimized fluorination reaction run in the absence of base. The shaded regions correspond to the resonances for the C–H starting material ( ; q, 2.61 ppm & t, 1.23 ppm) and C–F ( ; dq, 5.58 ppm & dd, 1.61 ppm), C–O ( ; s, 2.57 ppm [ketone] & d, 1.47 ppm [alcohol]), and C–N[4] ( ; q, 5.56 ppm & d, 1.62) products.

*Discussion of Scheme 2B (related to Figure S5):*

The observation of fluorinated product forming (0 to 3.5 h) and later being consumed (4 to 7 h) under the base-free reaction conditions (Scheme 2A and Figure S5) prompted exploration of NHSI-catalyzed acidolysis (Scheme 2B). Fluorination of ethyl benzene (following the general procedure in section II; 66% yield for this particular reaction), filtration through a silica plug (washed with DCE, 2 x 0.6 mL) and heating of the resulting solution of benzyl fluoride with added NHSI (89.2 mg, 0.3 mmol, 1 equiv) led to complete fluoride displacement in 10 minutes (70 °C). The benzyl fluoride was consumed quantitatively and afforded a 68% spectroscopic yield of sec-phenethyl alcohol relative to the benzyl fluoride product (corroborated by spiking the NMR sample with authentic alcohol).

A 4 mL scintillation vial was charged with $Li_2CO_3$ (201 mg, 2.7 mmol, 3 equiv), NFSI (711 mg, 2.25 mmol, 2.5 equiv), 1-bromo-4-ethylbenzene (126 µL, 0.9 mmol, 1 equiv), $CH_2Br_2$ (63 µL, 0.9 mmol, 1 equiv), $PhCF_3$ (111 µL, 0.9 mmol, 1 equiv), and a Teflon-coated magnetic stirbar on the bench top. The vial was sealed with a pierceable screw-on septum cap. Inside the glovebox, a BPhen$Cu^{I}$(OAc) stock solution was prepared by dissolving $Cu^{I}$(OAc) (32.6 mg, 0.265 mmol) and BPhen (105.6 mg, 0.318 mmol) in PhCl (26.4 mL). 1.8 mL of this deep red stock solution (2% $Cu^{I}$(OAc)/2.4% BPhen) was added to the reaction vial, resulting in an immediate color change to light blue/green. The vial was placed in a pre-heated block (45 °C) atop a stir plate set to 750 rpm. 50 µL aliquots were removed via microsyringe at the appropriate time intervals and processed identically to those above.

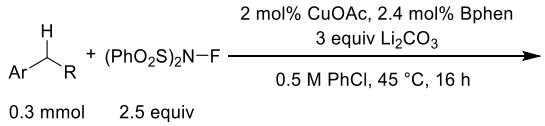



**Table S7.** Representative time course data for optimized fluorination reaction conditions run in the absence of $MeB(OH)_2$ (*cf.* Figure 1C).

| Time (h) | [C–H] (M) | [C–F] (M) | [C–$F_2$] (M) |
|---|---|---|---|
| 0.08 | 0.50 | 0.00 | 0.00 |
| 0.25 | 0.49 | 0.00 | 0.00 |
| 0.50 | 0.48 | 0.00 | 0.00 |
| 0.75 | 0.49 | 0.00 | 0.00 |
| 1.0 | 0.49 | 0.00 | 0.00 |
| 1.5 | 0.50 | 0.00 | 0.00 |
| 2.0 | 0.49 | 0.00 | 0.00 |
| 2.5 | 0.49 | 0.00 | 0.00 |
| 3.0 | 0.48 | 0.00 | 0.00 |

| Time (h) | [C–H] (M) | [C–F] (M) | [C–$F_2$] (M) |
|---|---|---|---|
| 3.5 | 0.49 | 0.00 | 0.00 |
| 4.0 | 0.49 | 0.00 | 0.00 |
| 4.5 | 0.49 | 0.00 | 0.00 |
| 5.0 | 0.49 | 0.00 | 0.00 |
| 6.0 | 0.50 | 0.00 | 0.00 |
| 7.0 | 0.50 | 0.00 | 0.00 |
| 8.0 | 0.50 | 0.00 | 0.00 |
| 12.0 | 0.50 | 0.00 | 0.00 |
| 16.0 | 0.52 | 0.00 | 0.00 |

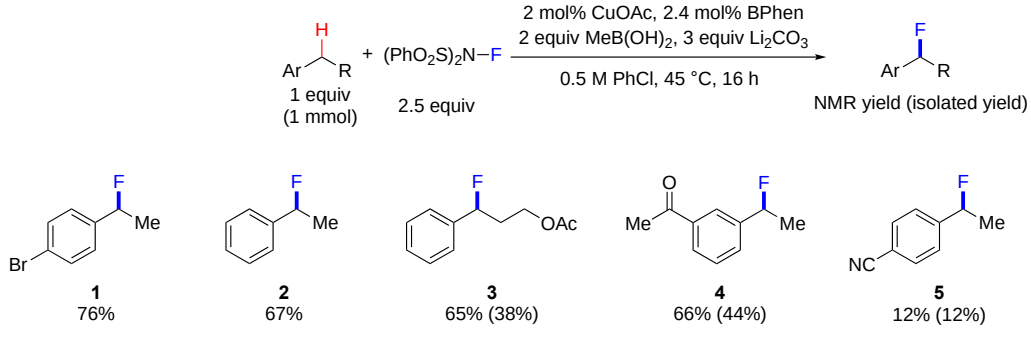
## V. Reaction Protocol and Characterization Data for Benzylic Fluorination on 1 mmol Scale

The optimized fluorination conditions were evaluated with a small series of benzylic C–H substrates on 1 mmol scale, with more thorough assessment of the synthetic scope and utility reported elsewhere.[5]

**Set-up:** On the benchtop, a disposable 20 mL glass vial was charged with $MeB(OH)_2$ (2 mmol, 120 mg, 2 equiv), $Li_2CO_3$ (3 mmol, 222 mg, 3 equiv), NFSI (2.5 mmol, 788 mg, 2.5 equiv), and a Teflon stir bar. The vial was sealed by a PTFE-lined pierceable cap. BPhen (0.024 mmol, 8.0 mg, 0.024 equiv) was weighed into a secondary vial with a Teflon stir bar. Both vials were then transferred to a purging glovebox under $N_2$(g). In the glovebox, CuOAc (0.02 mmol, 2.5 mg, 0.02 equiv) was weighed into the vial containing BPhen. Chlorobenzene (2 mL) was added to this vial and the red solution was stirred for 3 minutes. The C–H substrate (1.0 mmol, 1 equiv) was weighed into the vial containing the rest of the reaction components, and then the copper catalyst solution was transferred to the reaction vial. This reaction vial was then sealed and removed from the glovebox and set to stir at 45 °C on a stir plate at 450 rpm for 16 h.

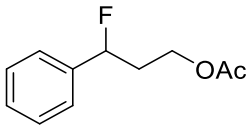
**Work-up:** The cap of the vial was loosened to vent the pressure build-up from the reaction. Dibromomethane (1 mmol, 70.2 µL, 1 equiv) and trifluorotoluene (1 mmol, 123 µL, 1 equiv) were then added as $^{1}H$ and $^{19}F$ NMR standards, respectively. The mixture was then diluted with $CDCl_3$ (0.6 mL), mixed, and a 30 µL aliquot was taken and filtered over a 1-inch celite plug directly into an NMR tube using 400 µL $CDCl_3$. The amount of benzyl fluoride product was then quantified relative to the two added internal standards. For purification, sodium dithionite (1 equiv with respect to the amount of NFSI used, ~150-250 mg) was added with 100 µL water directly to the reaction vial. The reaction was then stirred for 10 min to quench the remaining NFSI. The chunky mixture was then filtered over a 3-inch pad of silica into a disposable 24 mL glass vial using dichloromethane as the eluent. The vial was then carefully concentrated to prevent accidental evaporation of desired product and the remaining chlorobenzene solution was added directly to a silica gel column for separation of the product by column chromatography (0% pentane to 10% EtOAc, followed by ramping). Concentration of the product-containing fractions allows collection of the final product.

**Table S8. Summary of Cu/NFSI Benzylic C–H Fluorination Data**



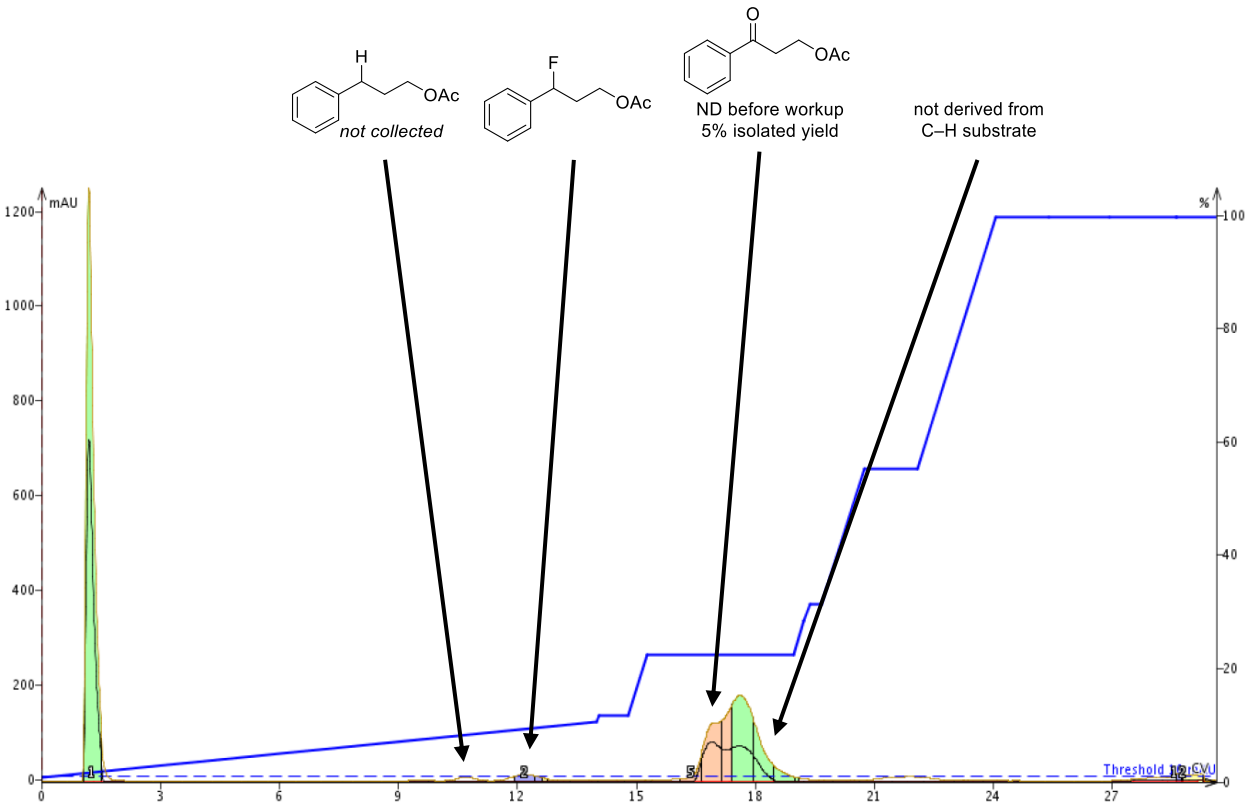

Purified isolated products were obtained in a few cases, but typically in reduced yield relative to the NMR yields owing to conversion of the benzyl fluoride during isolation (NMR yields were obtained with $CH_2Br_2$ and $PhCF_3$ as $^1H$ and $^{19}F$ internal standards, respectively).

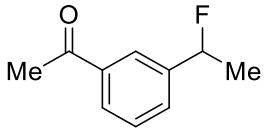
*Product Isolations:*



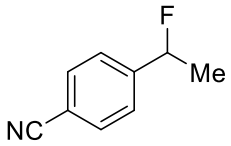

**(1) 3-fluoro-3-phenylpropyl acetate:** Prepared from 3-phenylpropyl acetate (1 mmol, 178 mg, 1 equiv) according to the reaction protocol in section V.
Isolated Yield: 38%, 73.6 mg of clear liquid (65% NMR yield).
Product Spectra Available in the Literature (CAS): Yes[6] (412026-80-3)
**$^{1}$H NMR** ($CDCl_3$, 500 MHz): δ 7.42 – 7.32 (m, 5H), 5.57 (ddd, J = 47.8, 8.7, 4.2 Hz, 1H), 4.26 (ddd, J = 11.2, 8.0, 5.6 Hz, 1H), 4.20 (dt, J = 11.3, 5.9 Hz, 1H), 2.30 (tdt, J = 14.6, 8.8, 5.6 Hz, 1H), 2.23 – 2.09 (m, 1H), 2.05 (s, 3H).
**$^{13}$C NMR** ($CDCl_3$, 126 MHz): δ 170.9, 139.5 (d, J = 19.5 Hz), 128.6, 128.5 (d, J = 2.0 Hz), 125.5 (d, J = 6.7 Hz), 91.4 (d, J = 170.9 Hz), 60.5 (d, J = 4.9 Hz), 36.2 (d, J = 24.1 Hz), 20.9.
**$^{19}$F NMR** ($CDCl_3$, 377 MHz): δ -177.42.

The chromatogram below is provided to show some of the characterized side products formed in the process of isolation, which resulted in a reduced isolated yield relative to the NMR yield.

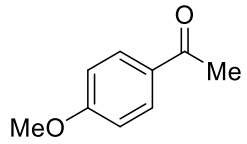





**(2) 1-(3-(1-fluoroethyl)phenyl)ethan-1-one:** Prepared from 1-(3-ethylphenyl)ethan-1-one (1 mmol, 148 mg, 1 equiv) according to the reaction protocol in section V.
Isolated Yield: 44%, 72.4 mg of clear liquid (66% NMR yield).
Product Spectra Available in the Literature (CAS): No (1550969-43-1)
**$^{1}$H NMR** ($CDCl_3$, 600 MHz): δ 7.95 – 7.88 (m, 2H), 7.59 – 7.54 (m, 1H), 7.48 (t, J = 7.7 Hz, 1H), 5.68 (dq, J = 47.5, 6.5 Hz, 1H), 2.62 (s, 3H), 1.66 (dd, J = 24.0, 6.5 Hz, 3H).
**$^{13}$C NMR** ($CDCl_3$, 150 MHz): δ 197.8, 142.2 (d, J = 19.9 Hz), 137.3, 129.8 (d, J = 6.8 Hz), 128.9, 128.2 (d, J = 1.8 Hz), 124.9 (d, J = 7.0 Hz), 90.4 (d, J = 168.9 Hz), 26.7, 23.0 (d, J = 24.9 Hz).
**$^{19}$F NMR** ($CDCl_3$, 377 MHz): δ -168.91.
**HRMS (ESI) m/z:** $[M+H]^+$ Calcd for $C_{10}H_{12}FO$ 167.0867; Found 167.0868.



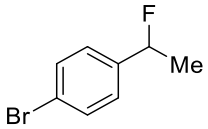

**(3) 4-(1-fluoroethyl)benzonitrile:** Prepared from 4-ethylbenzonitrile (1 mmol, 131 mg, 1 equiv) according to the reaction protocol in section V.
Isolated Yield: 12%, 18.6 mg of clear liquid (12% NMR yield).
Product Spectra Available in the Literature (CAS): Yes[6] (155671-14-0)
**$^{1}$H NMR** ($CDCl_3$, 500 MHz): δ 7.67 (d, J = 7.7 Hz, 2H), 7.45 (d, J = 8.7 Hz, 2H), 5.67 (dq, J = 47.4, 6.5 Hz, 1H), 1.64 (dd, J = 24.0, 6.5 Hz, 3H).
**$^{13}$C NMR** ($CDCl_3$, 126 MHz): δ 146.7 (d, J = 19.9 Hz), 132.4, 125.6 (d, J = 7.6 Hz), 118.5, 112.0 (d, J = 1.9 Hz), 89.8 (d, J = 171.3 Hz), 22.9 (d, J = 24.5 Hz).
**$^{19}$F NMR** ($CDCl_3$, 377 MHz): δ -172.70.




*no C–F bond detected*

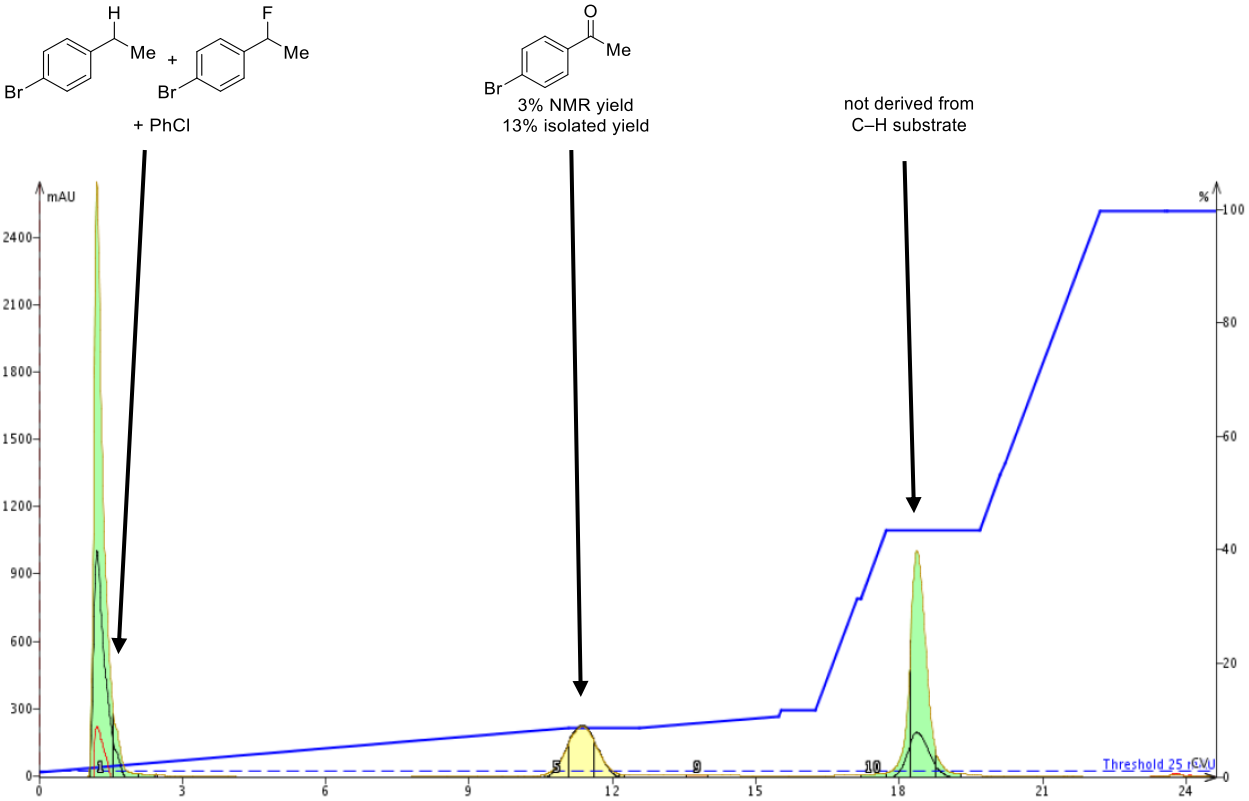
**(4) 1-(4-methoxyphenyl)ethan-1-one:** Prepared from 4-ethylanisole (1 mmol, 136 mg, 1.0 equiv) according to the reaction protocol in section V.
Isolated Yield: 96%, 144.7 mg of colorless solid (97% NMR yield).
Product Spectra Available in the Literature (CAS): Yes[7] (100-06-1)
**$^{1}$H NMR** ($CDCl_3$, 500 MHz): δ 7.94 (d, *J* = 8.8 Hz, 2H), 6.93 (d, *J* = 8.8 Hz, 2H), 3.87 (s, 3H), 2.55 (s, 3H).
**$^{13}$C NMR** ($CDCl_3$, 126 MHz): δ 196.8, 163.5, 130.6, 130.4, 113.7, 55.5, 26.3.

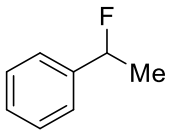
*Products that were not successfully isolated:*




**(5) 1-bromo-4-(1-fluoroethyl)benzene:** Prepared from 1-bromo-4-ethylbenzene (1 mmol, 185 mg, 1 equiv) according to the reaction protocol in section V, but was not successfully isolated. See section VII for a crude reaction NMR spectrum.
Product Spectra Available in the Literature (CAS): Yes[8] (159298-87-0)
**Benzyl Fluoride C–H Shift:** $^{1}$H NMR ($CDCl_3$, 400 MHz): δ 5.59 (dq, J = 47.5, 6.4 Hz).
Calibrated $^{1}$H NMR Yield from Benzyl Proton: 77%
**Benzylic Fluoride Shift:** $^{19}$F NMR ($CDCl_3$, 377 MHz): δ -168.01.
Calibrated $^{19}$F NMR Yield from Benzyl Fluoride: 75%
**Benzyl Difluoride Fluorine Shift:** $^{19}$F NMR ($CDCl_3$, 377 MHz): δ -87.78.
Calibrated $^{19}$F NMR Yield of Benzyl Difluoride: 3%

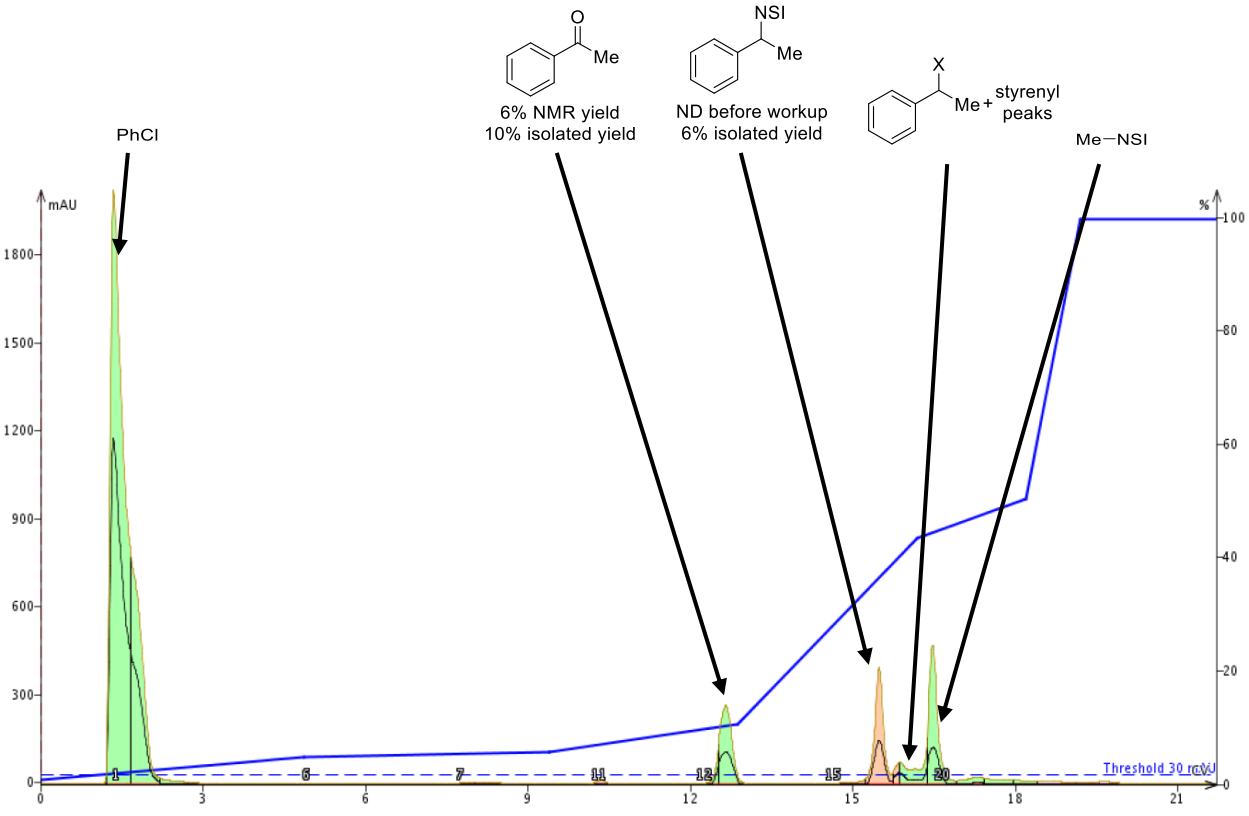
Purification: Normal phase silica gel chromatography was used with a gradient of 0%→10% EtOAc in pentane. The chromatogram below is provided to show what was obtained from attempted isolation. Significant acetophenone formation was observed after the NFSI quench and chromatography and the product was not readily separable from the starting material and chlorobenzene.






**(6) (1-fluoroethyl)benzene:** Prepared from ethylbenzene (1 mmol, 106 mg, 1.0 equiv) according to the reaction protocol in section V, but was not successfully isolated . See section VII for a crude reaction NMR spectrum.
Product Spectra Available in the Literature (CAS): Yes[9] (7100-97-2)
**Benzyl Fluoride C–H Shift:** $^{1}$H NMR ($CDCl_3$, 400 MHz): δ 5.63 (dq, J = 47.7, 6.5 Hz).
Calibrated $^{1}$H NMR Yield from Benzyl Proton: 66%
**Benzylic Fluoride Shift:** $^{19}$F NMR ($CDCl_3$, 377 MHz): δ -167.03.
Calibrated $^{19}$F NMR Yield from Benzyl Fluoride: 67%
**Benzyl Difluoride Fluorine Shift:** $^{19}$F NMR ($CDCl_3$, 377 MHz): δ -87.63.
Calibrated $^{19}$F NMR Yield of Benzyl Difluoride: 6%

Purification: Normal phase silica gel chromatography was used with a gradient of 0%→10% EtOAc in pentane. The chromatogram below is provided to show what was obtained from attempted isolation. No desired product was observed in any column fractions, and numerous new side products were formed.



## VI. References


1) Chen, L.; Lang, H.; Fang, L.; Yu, J.; Wang, L. Nickel-Catalyzed Desulfitative Suzuki-Miyaura Cross-Coupling of *N*,*N*-Disulfonylmethylamines and Arylboronic Acids. *Eur. J. Org. Chem.* **2014**, *29*, 6385-6389.

2) Vantourout, J. C.; Miras, H. N.; Isidro-Llobet, A.; Sproules, S.; Watson, A. J. B. Spectroscopic Studies of the Chan-Lam Amination: A Mechanism-Inspired Solution to Boronic Ester Reactivity. *J. Am. Chem. Soc.* **2017**, *139*, 4769-4779.

3) Rossi, S. A.; Shimkin, K. W.; Xu, Q.; Mori-Quiroz, L. M.; Watson, D. A. Selective Formation of Secondary Amides via the Copper-Catalyzed Cross-Coupling of Alkylboronic Acids with Primary Amides. *Org. Lett.* **2013**, *15*, 2314-2317.

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5 ) Vasilopoulos, A.; Golden, D. L.; Buss, J. A.; Stahl, S. S. Copper-Catalyzed C–H Fluorination/Functionalization Sequence Enabling Benzylic C–H Cross Coupling with Diverse Nucleophiles. *Org. Lett.*, submitted for publication.

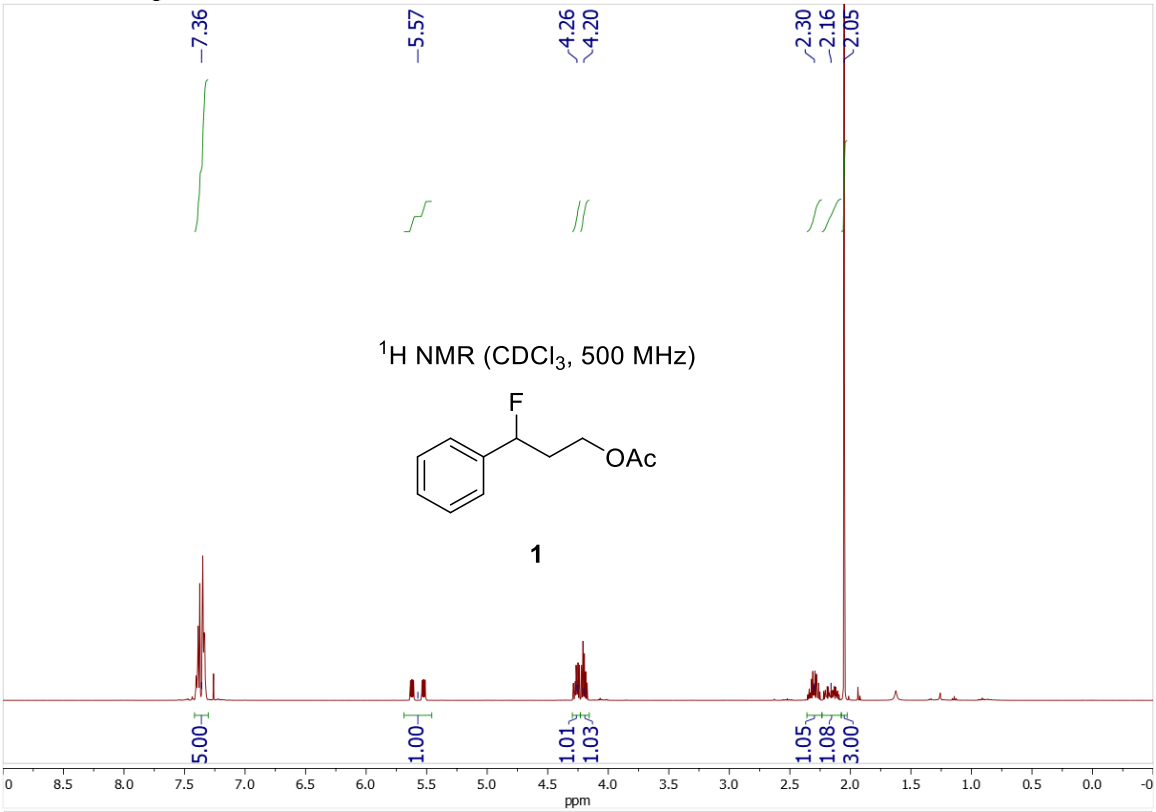
6) Xia, J.-B.; Zhu, C.; Chen, C. Visible Light-Promoted Metal-Free C–H Activation: Diarylketone-Catalyzed Selective Benzylic Mono- and Difluorination. *J. Am. Chem. Soc.* **2013**, *135*, 17494-17500.

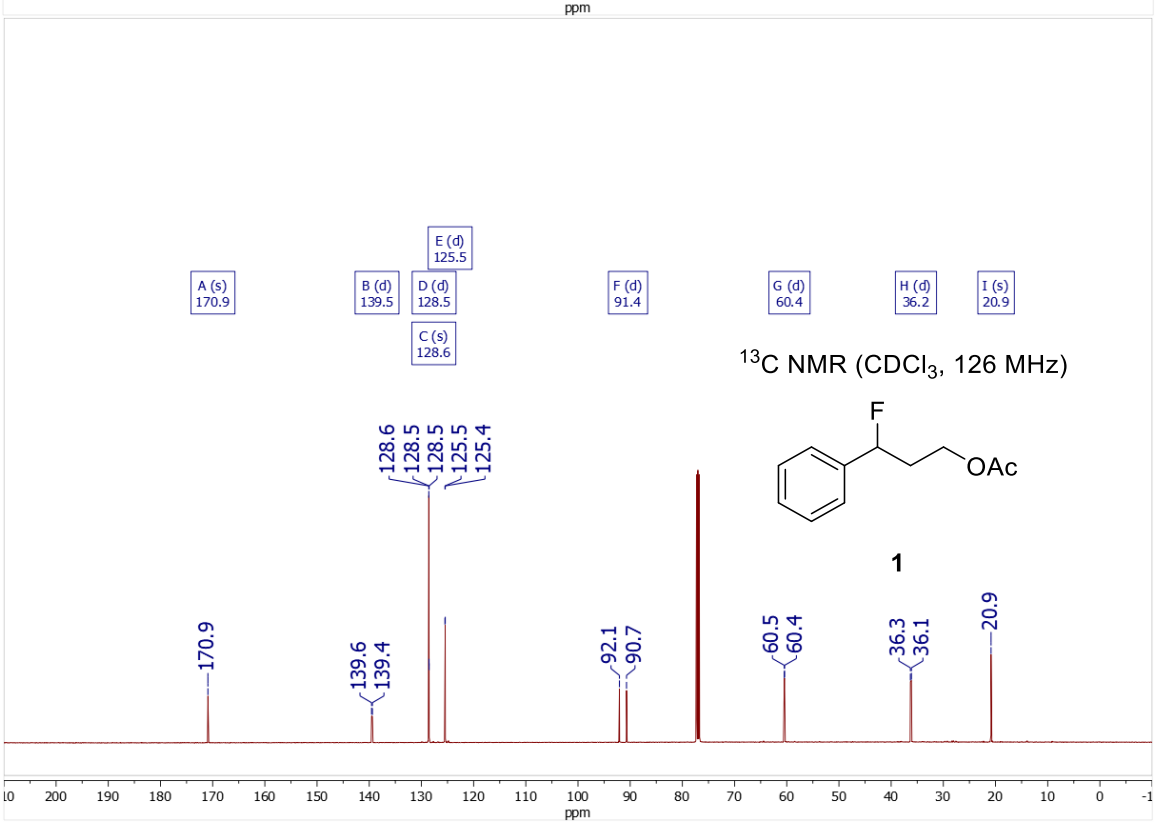
7) SDBSWeb. https://sdbs.db.aist.go.jp/sdbs/cgi-bin/landingpage?sdbsno=1164 (accessed Jun 30, **2020**), National Institute of Advanced Industrial Science and Technology.

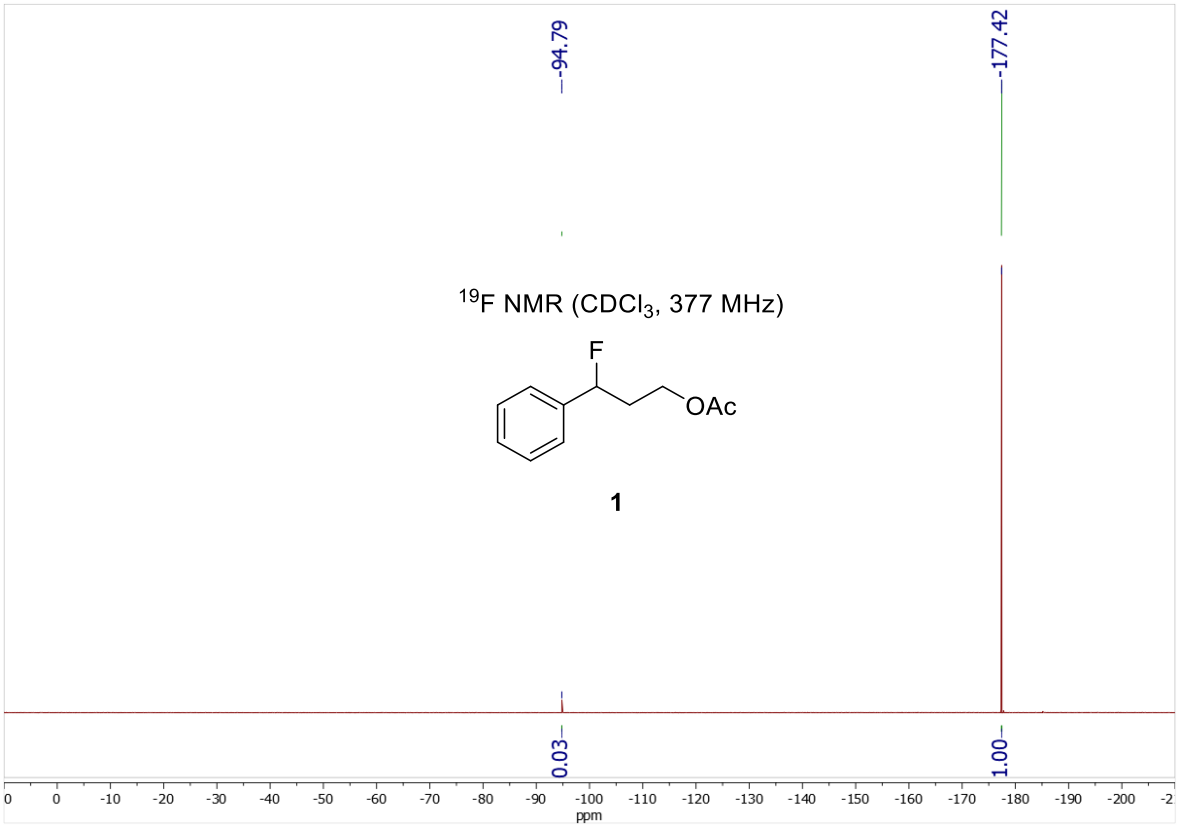
8) Liu, W.; Groves, J.T. Manganese-Catalyzed Oxidative Benzylic C–H Fluorination by Fluoride Ions. *Angew. Chem. Int. Ed.* **2013**, *52*, 6024-6027.

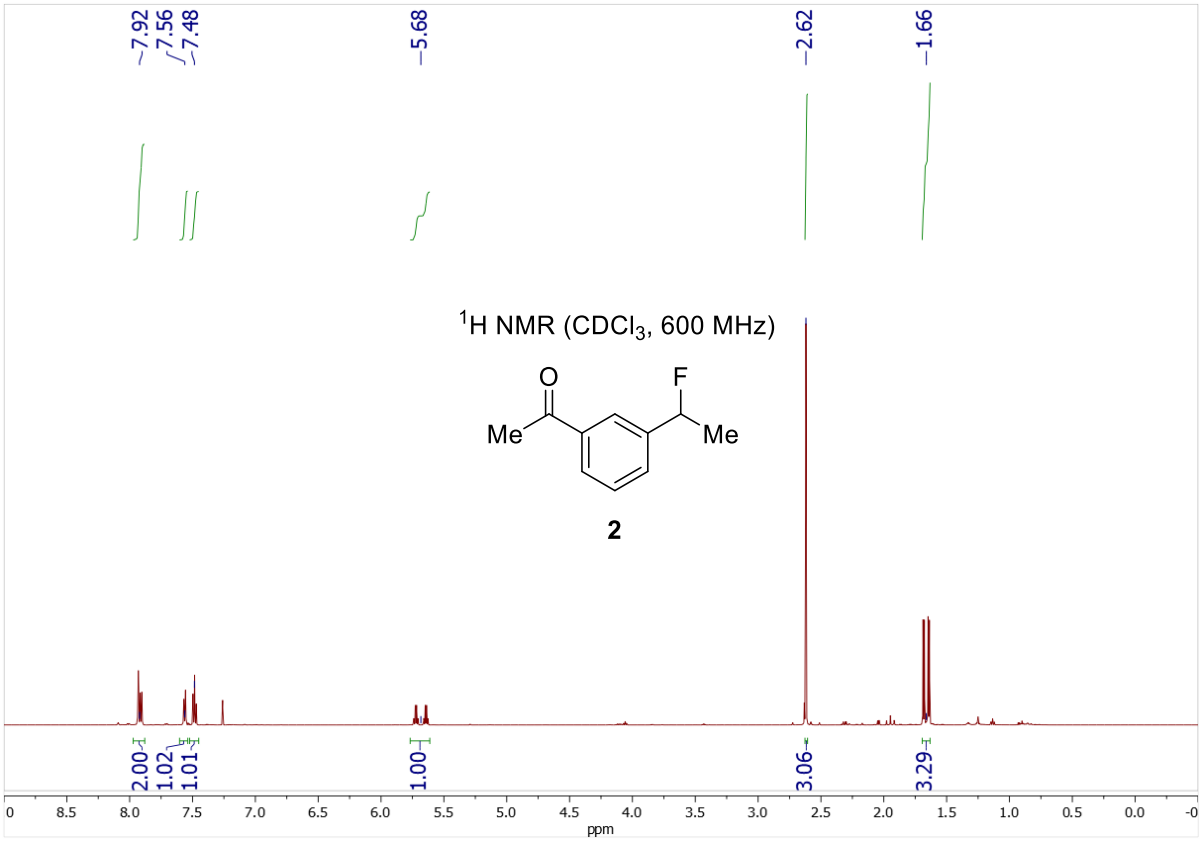
9) Bloom, S.; Pitts, C. R.; Woltornist, R.; Griswold, A.; Holl, M. G.; Lectka, T. Iron(II)-Catalyzed Benzylic Fluorination. *Org. Lett.* **2013**, *15*, 1722-1724.

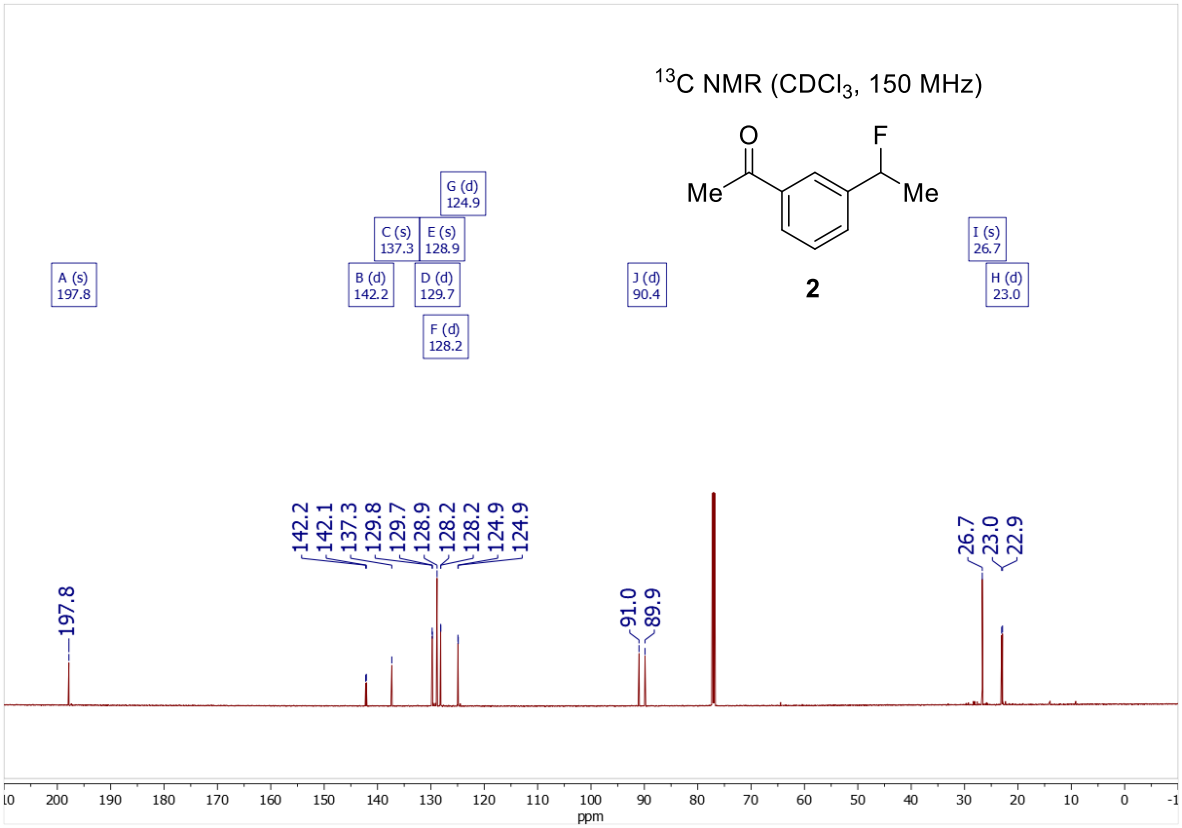
## VII. NMR Spectra

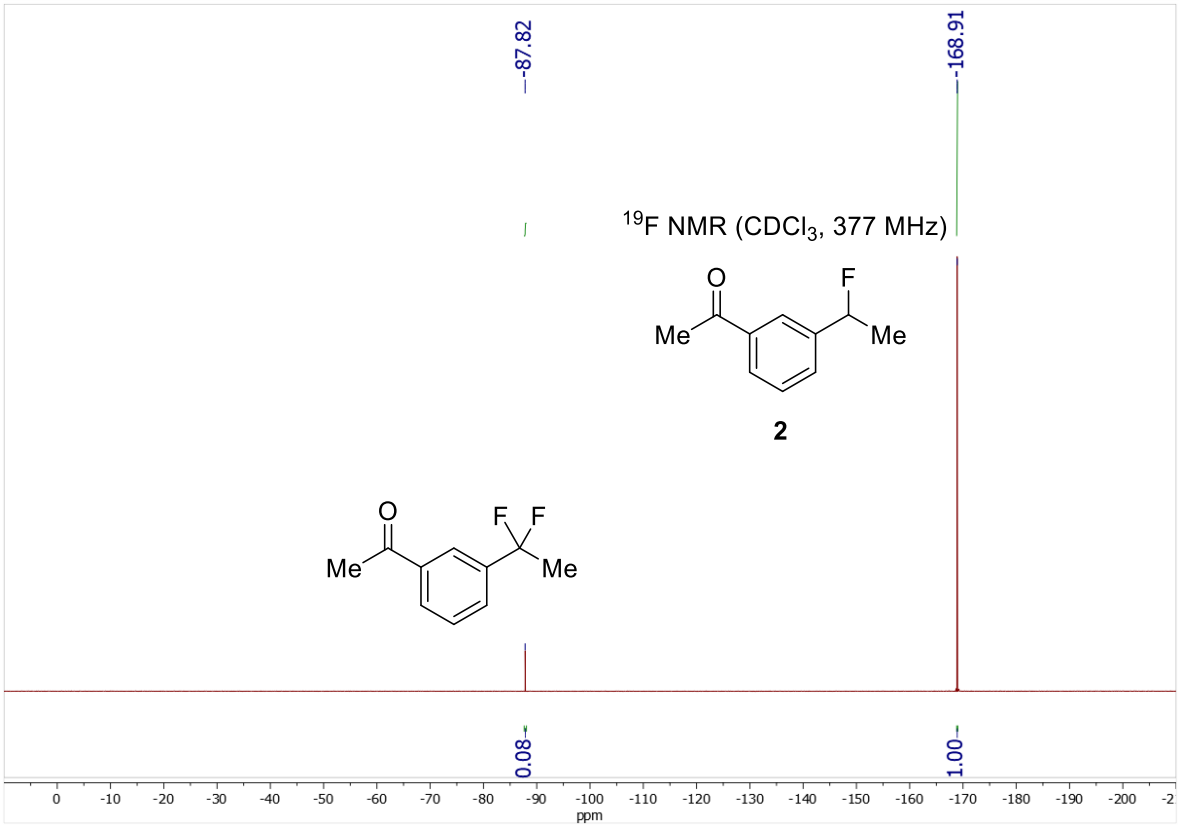


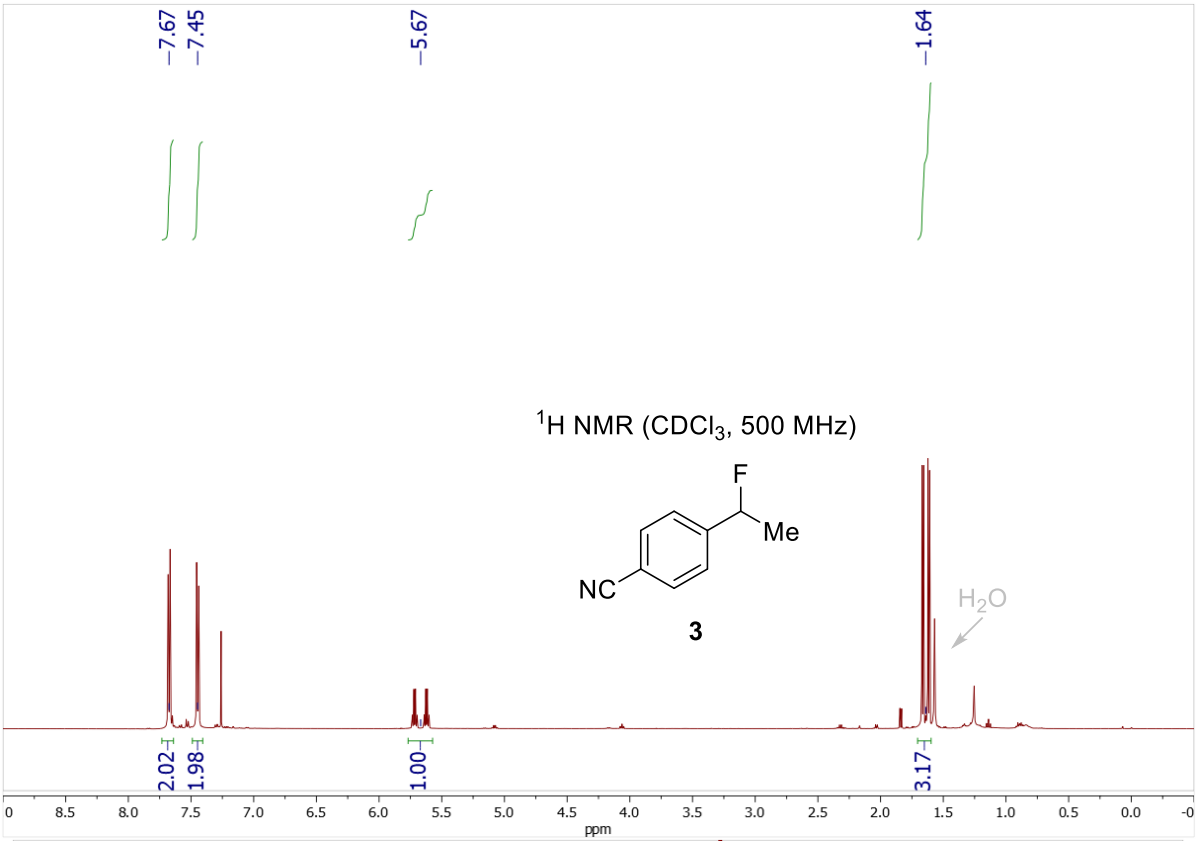



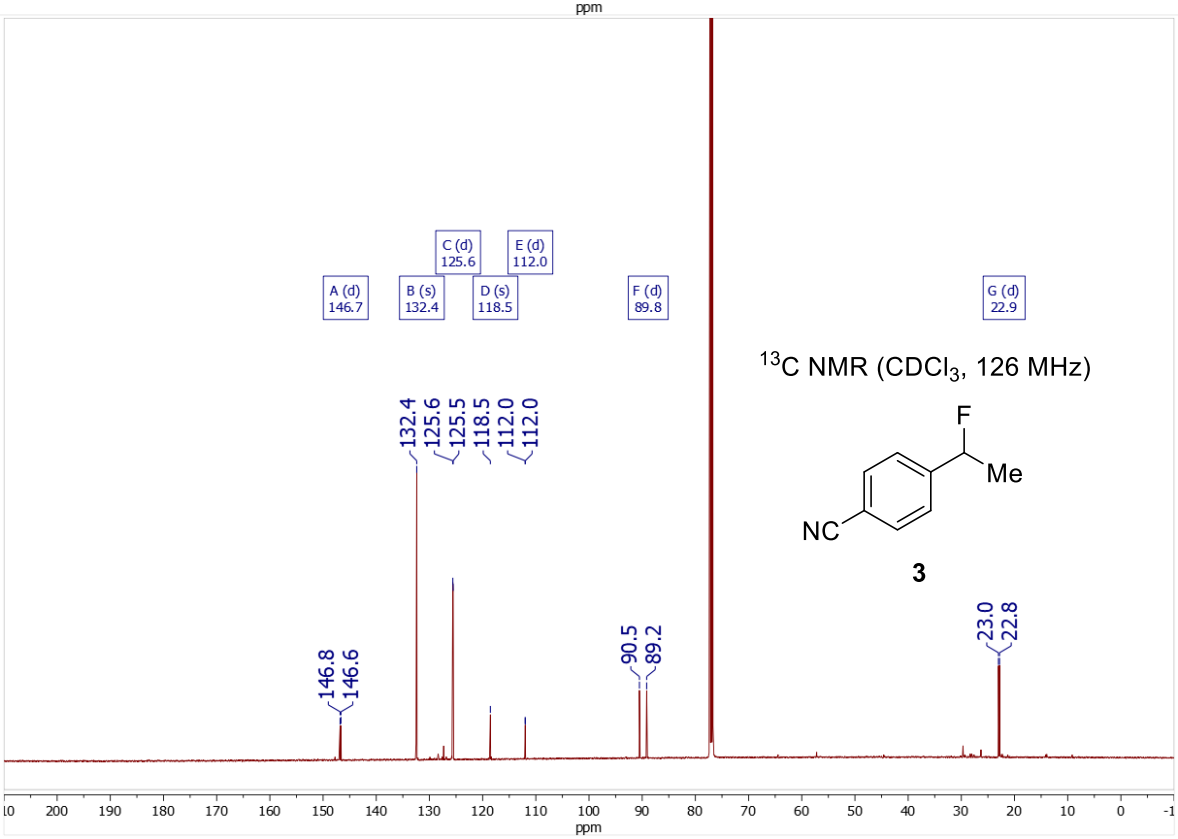

-94.79
-177.42
$^{19}$F NMR ($CDCl_3$, 377 MHz)
F
OAc
1
0.03
1.00
ppm

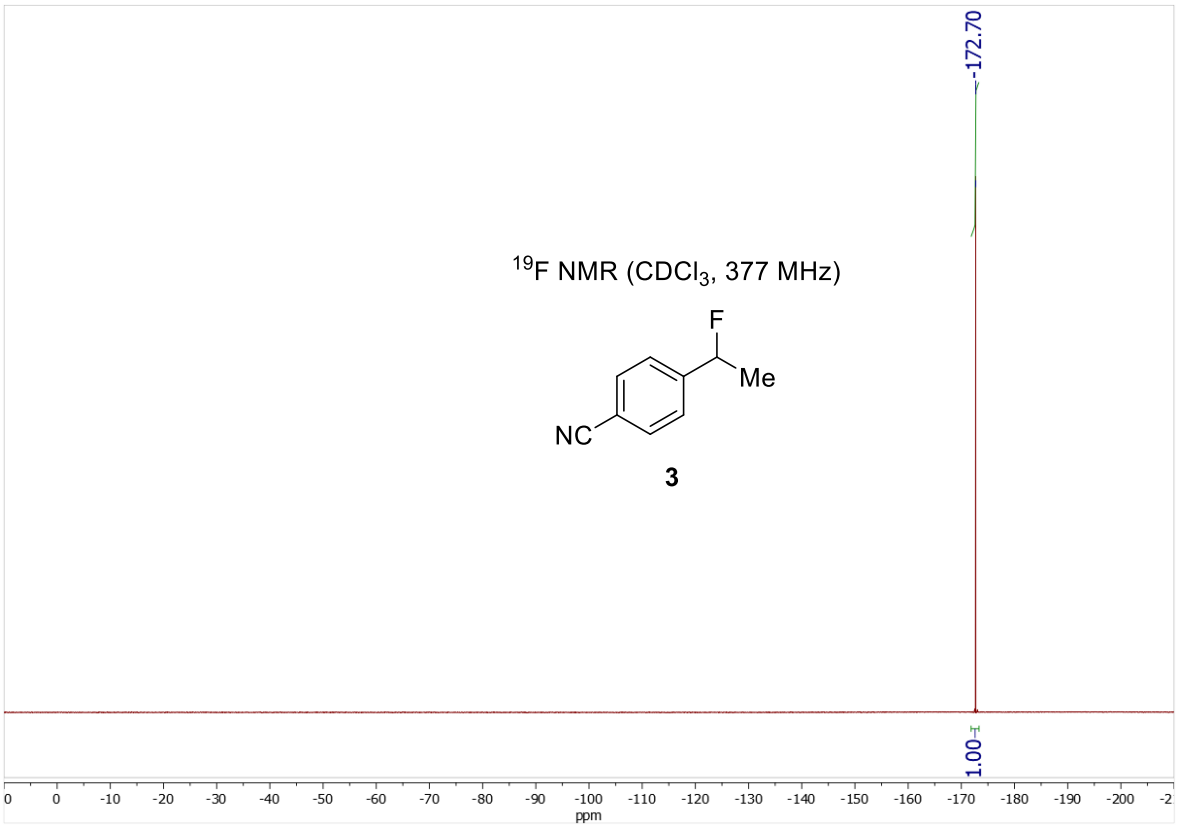

7.92
7.56
7.48
5.68
2.62
1.66
$^{1}$H NMR ($CDCl_3$, 600 MHz)
O
F
Me
Me
2
2.00
1.02
1.01
1.00
3.06
3.29
ppm

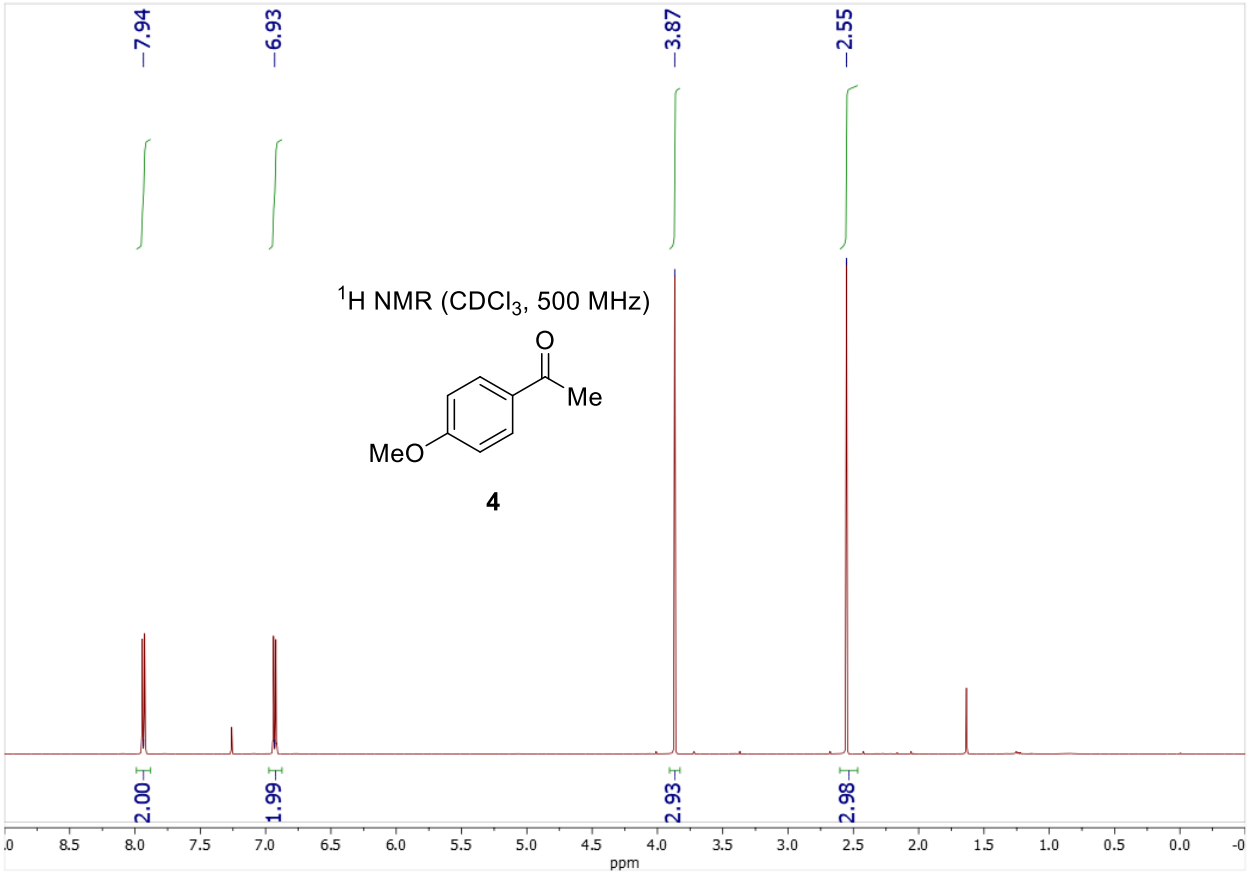

$^{13}$C NMR ($CDCl_3$, 150 MHz)
O
F
Me
Me
2
A (s) 197.8
B (d) 142.2
C (s) 137.3
D (d) 129.7
E (s) 128.9
F (d) 128.2
G (d) 124.9
J (d) 90.4
I (s) 26.7
H (d) 23.0
197.8
142.2
142.1
137.3
129.8
129.7
128.9
128.2
128.2
124.9
124.9
91.0
89.9
26.7
23.0
22.9
ppm

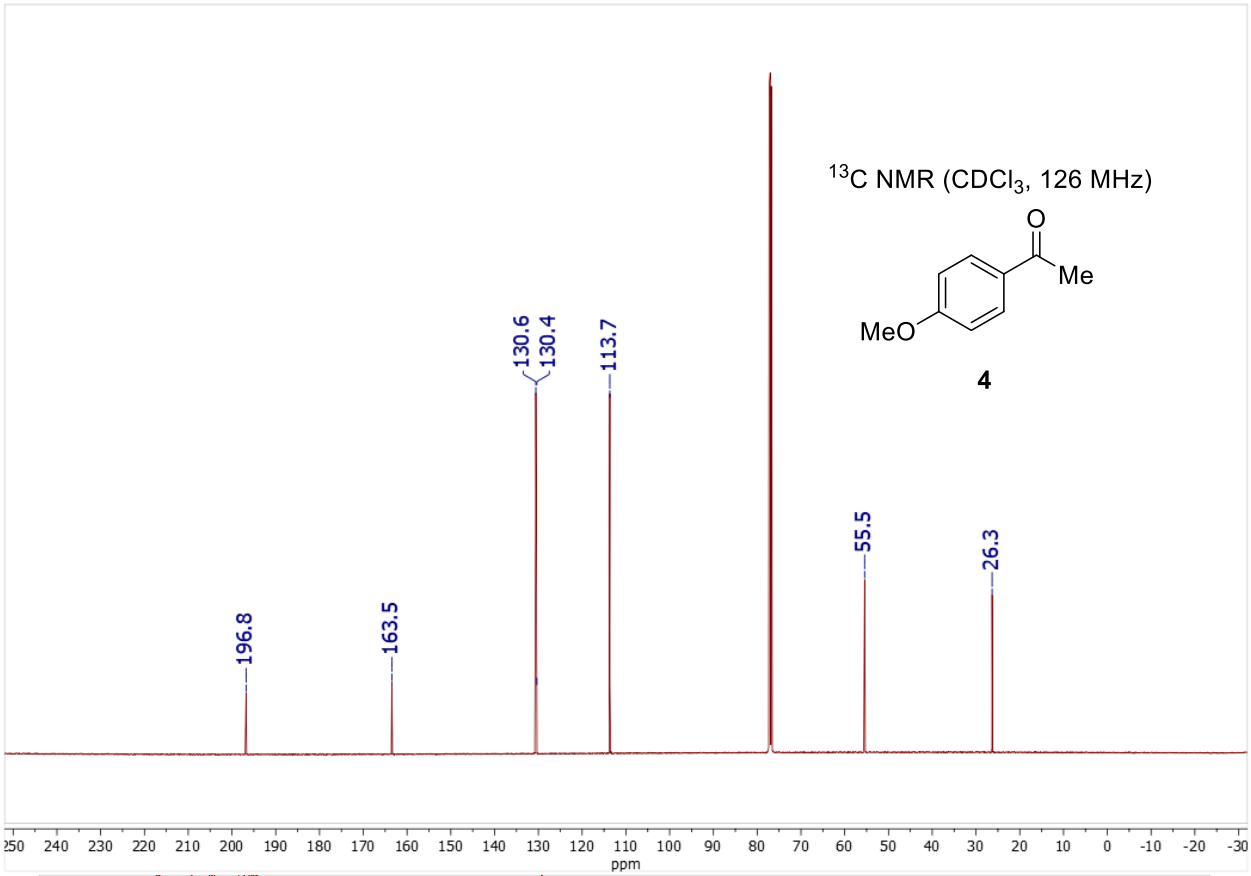

-87.82
-168.91
$^{19}$F NMR ($CDCl_3$, 377 MHz)
O
F
Me
Me
2
O
F
F
Me
Me
0.08
1.00
ppm

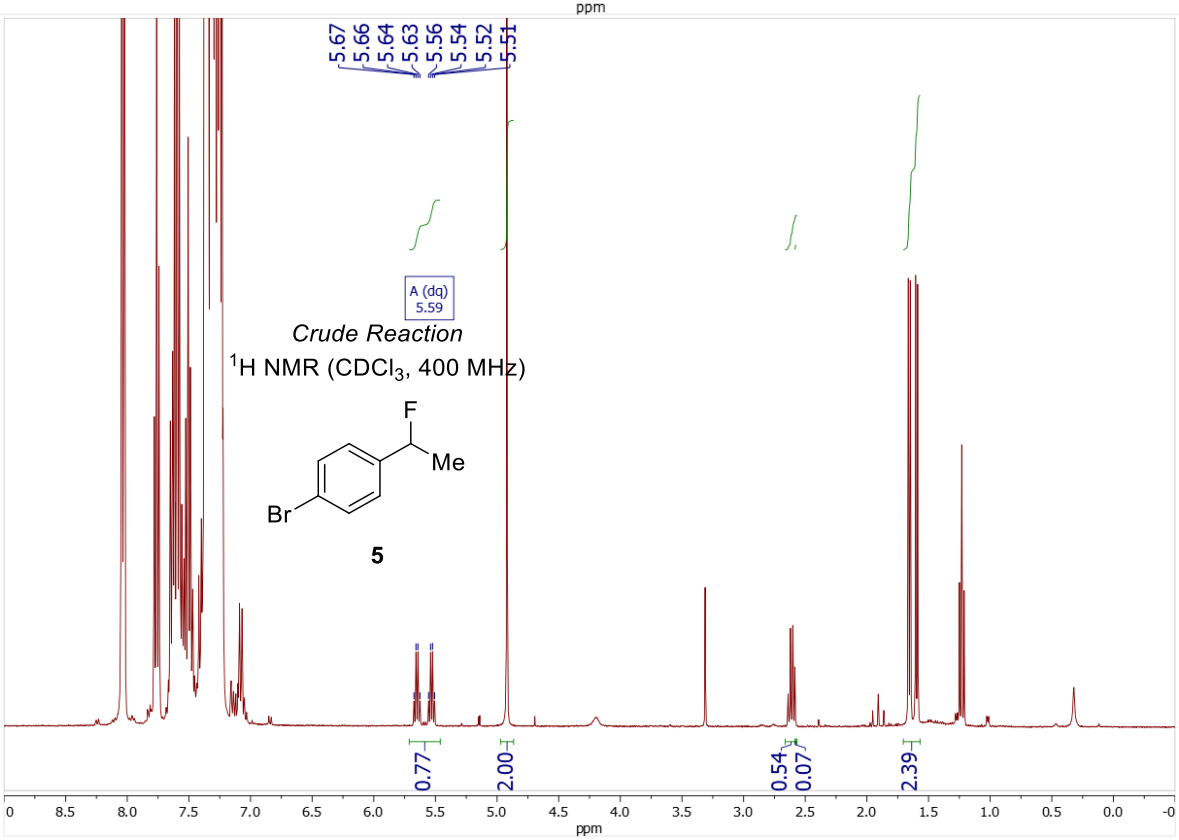

7.67
7.45
5.67
1.64
$^1$H NMR ($CDCl_3$, 500 MHz)
F
Me
NC
3
$H_2O$
2.02
1.98
1.00
3.17
ppm

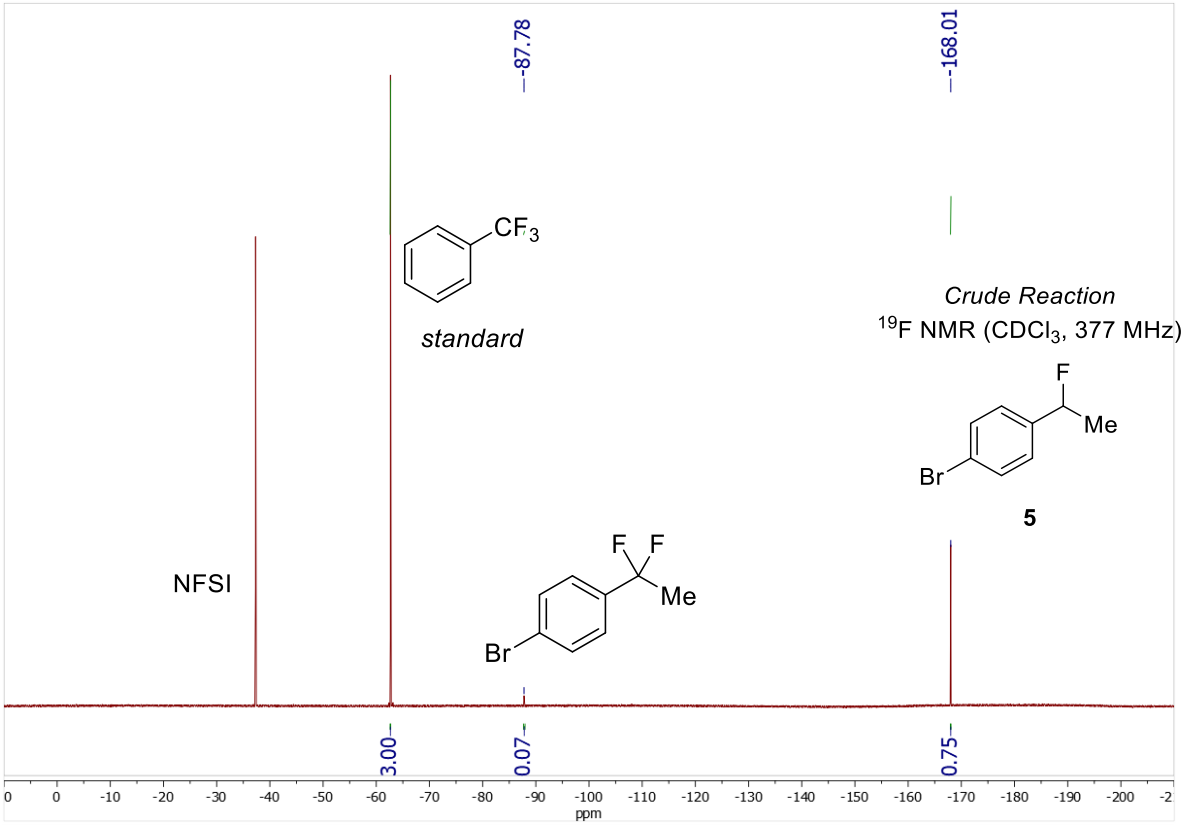

A (d) 146.7
B (s) 132.4
C (d) 125.6
D (s) 118.5
E (d) 112.0
F (d) 89.8
G (d) 22.9
$^{13}$C NMR ($CDCl_3$, 126 MHz)
132.4
125.6
125.5
118.5
112.0
112.0
146.8
146.6
90.5
89.2
23.0
22.8
F
Me
NC
3
ppm

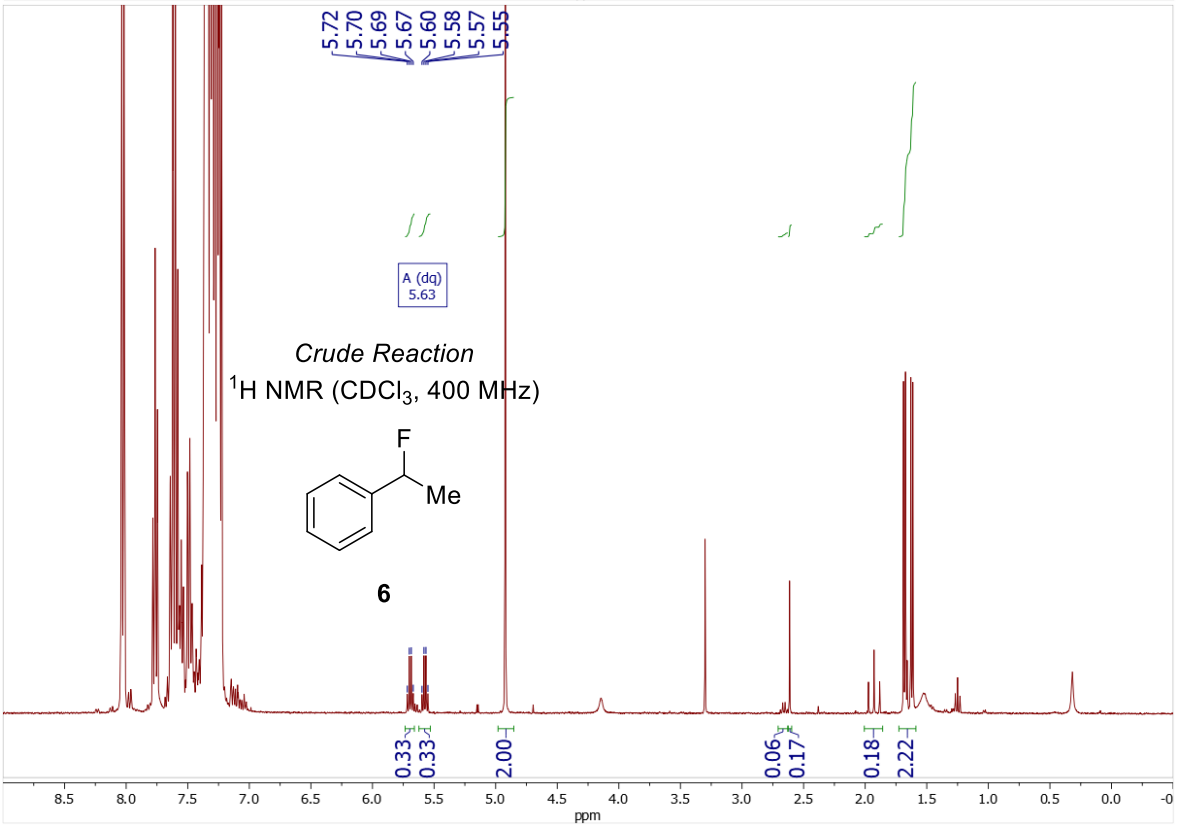

-172.70
19F NMR (CDCl3, 377 MHz)
F
Me
NC
3
1.00
0 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -2
ppm

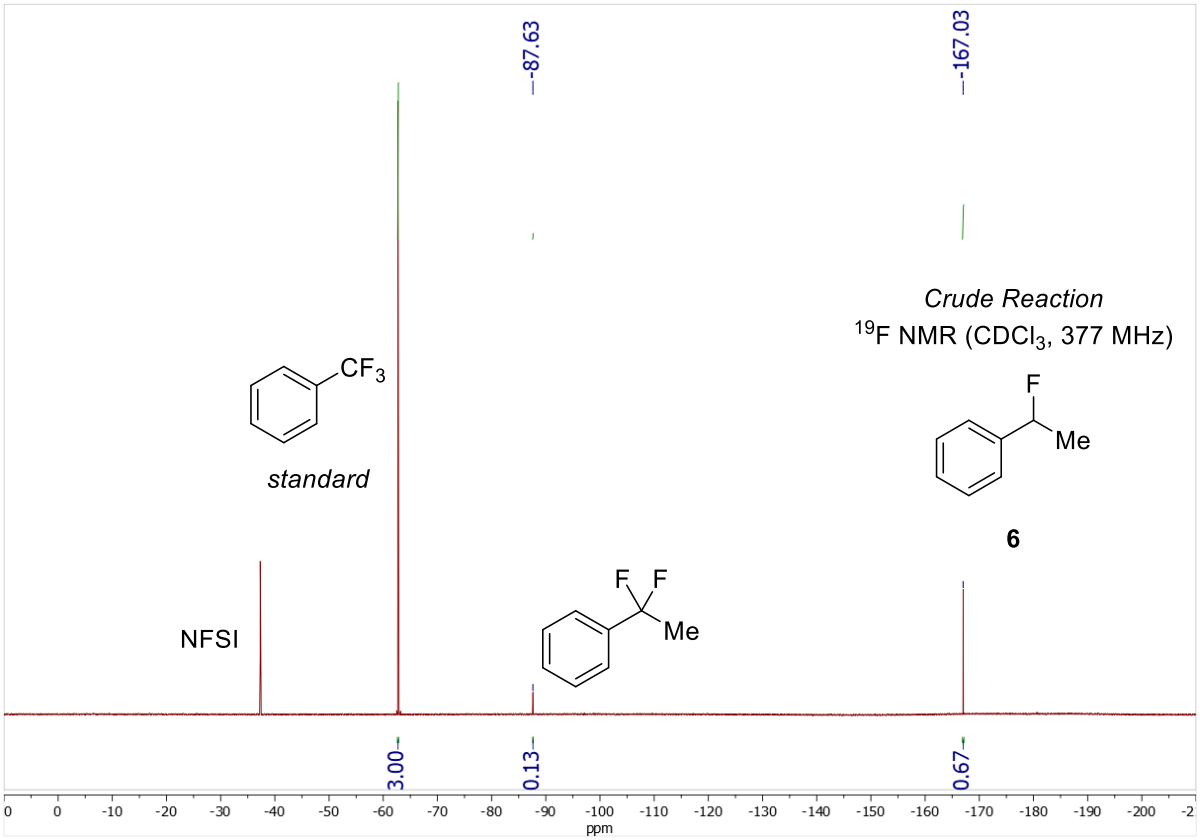

7.94
6.93
3.87
2.55
1H NMR (CDCl3, 500 MHz)
O
Me
MeO
4
2.00
1.99
2.93
2.98
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm


$^{13}$C NMR ($CDCl_3$, 126 MHz)
O
Me
MeO
4
196.8
163.5
130.6
130.4
113.7
55.5
26.3
ppm


5.67
5.66
5.64
5.63
5.56
5.54
5.52
5.51
A (dq)
5.59
Crude Reaction
$^1$H NMR ($CDCl_3$, 400 MHz)
F
Me
Br
5
0.77
2.00
0.54
0.07
2.39
ppm


-87.78
-168.01
CF3
standard
Crude Reaction
19F NMR (CDCl3, 377 MHz)
F
Me
Br
5
NFSI
F F
Me
Br
3.00
0.07
0.75
ppm


5.72
5.70
5.69
5.67
5.60
5.58
5.57
5.55
A (dq)
5.63
Crude Reaction
1H NMR (CDCl3, 400 MHz)
F
Me
6
0.33
0.33
2.00
0.06
0.17
0.18
2.22
ppm


-87.63
-167.03
Crude Reaction
19F NMR (CDCl3, 377 MHz)
CF3
standard
F
Me
6
NFSI
F F
Me
3.00
0.13
0.67
0 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -2
ppm